

# Reducing antibiotics for respiratory tract symptoms in primary care: consolidating 'why' and considering 'how'

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## SUMMARY

We summarize recently published evidence showing that antibiotic treatment offers little or no benefit to most patients presenting with sore throats, acute otitis media, maxillary sinusitis, and acute bronchitis. Despite this research, the prescription of antibiotics for respiratory tract conditions is rising in Britain. This wastes money, encourages people to consult for self-limiting conditions, and causes bacteria to become resistant to antimicrobials. Ways of changing present practice are under-researched. Enhanced consulting skills, guidelines and monitoring strategies, patient education, and anti-inflammatory drugs for recurrent and chronic sufferers all hold promise.

**Key words:** overprescribing; antibiotics; respiratory tract infections.

## Introduction

It is now recognized that antibiotics only modify slightly the course of throat infections.<sup>1-5</sup> Several research reports have recently demonstrated that the same is also true for acute otitis media,<sup>6</sup> maxillary sinusitis,<sup>7-9</sup> and acute bronchitis.<sup>10-14</sup> European and American studies show that between 44% and 90% of children and adults consulting for colds, upper respiratory tract infections (URTIs) and acute bronchitis receive a prescription for antibiotics.<sup>15-22</sup> Over 90% of children in most developed countries presenting with acute otitis media are prescribed antibiotics.<sup>23</sup> Antibiotic prescribing for respiratory tract infections is rising in Britain,<sup>24</sup> and newer, more expensive, broader spectrum antibiotics are being prescribed more often.<sup>24,25</sup>

However, identifying and implementing effective solutions is still under-researched.<sup>15,16,26</sup> In this review, we summarize recent evidence about the effectiveness of antibiotics for a range of infections at various sites in the respiratory tract, highlight problems caused by present prescribing patterns, and consider possible directions for solutions.

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## Evidence favouring more restrictive use of antibiotics in primary care

We searched for randomized, placebo-controlled trials and secondary analyses of trials of antibiotic treatment for pharyngitis, tonsillitis, acute otitis media, maxillary sinusitis, and acute bronchitis. We included only those studies published in the past five years, and limited our search to four major general medical journals (*Lancet*, *British Medical Journal*, *New England Journal of Medicine*, and *Journal of the American Medical Association*) and four major primary care journals (*British Journal of General Practice*, *Family Medicine*, *Journal of Family Practice*, and *Archives of Family Medicine*). We also searched the Cochrane Database for relevant systematic reviews. Our findings are summarized in Table 1.

Despite one of the three well-conducted trials for sinusitis showing a clear benefit for antibiotic treatment,<sup>27</sup> the overall message is clear: for most people in developed countries with these infections, antibiotics do not significantly shorten the duration of acute symptoms or prevent complications. For example, Little *et al*<sup>28</sup> reviewed the evidence for preventing rheumatic fever and acute nephritis through the routine prescription of penicillin for sore throats. The probability of preventing one case is the same as causing a death by penicillin-induced anaphylaxis.

Furthermore, antibiotic treatment may cause as much morbidity as it reduces: for every child with otitis media treated with antibiotics who experiences diminished pain between two and seven days, three other children will have vomiting, diarrhoea, or a rash without deriving any benefit.<sup>6,29</sup> For bronchitis, the probability of obtaining benefit from antibiotics may be similar to the probability of being harmed by them.<sup>12,13</sup>

## The consequences of present prescribing

### Financial implications

The Audit Commission has identified £77 million in potential savings to be made from the rational prescription of antibiotics in primary care.<sup>30</sup> If antibiotic treatment for otitis media was delayed for 24 hours in those with otalgia in the United Kingdom, 1.84 million fewer prescriptions for antibiotics would be issued, saving around £6 million a year.<sup>31</sup> The costs of consultations alone for sore throats is approximately £60 million a year.<sup>28</sup> The annual cost of consultations for URTIs in Ontario, Canada, has been estimated at £200 million.<sup>32</sup> In the United States, \$37.5 million is spent on antibiotics for colds each year,<sup>16</sup> and the costs of physician visits and antibiotic treatment for acute bronchitis has been estimated to be between \$200 million and \$300 million annually.<sup>10</sup>

### Effects on help-seeking behaviour

Receiving antibiotics reinforces patients' perceptions that they should consult for similar problems in the future, and their expectation of receiving a prescription.<sup>30</sup> A survey study in the US found that reported previous antibiotic usage has a strong relationship with belief in the effectiveness of antibiotics for URTIs.<sup>33</sup> In the UK, prescribing antibiotics for sore throats was

**Table 1.** Summary of placebo-controlled trials and secondary studies from selected general medical and primary care journals and the Cochrane Data Base of Systematic Reviews published in the past five years of antibiotic treatment for sore throat, acute otitis media, maxillary sinusitis, and acute bronchitis.

Authors and publication year	Condition	Type of study	Subjects	Interventions	Outcome	Side effects
Howe <i>et al</i> <sup>5</sup>	Sore throat	RCT	145 patients with sore throat	Penicillin, cefixime, and placebo	Symptom resolution by day three greater in cefixime group than placebo. Penicillin did not improve symptom resolution by day three, and cefixime not significantly different from placebo	No differences between intervention groups in stopping medication because of side effects
Del Mar <i>et al</i> <sup>1</sup>	Sore throat	Systematic review	18 studies, 9189 subjects with sore throat	Antibiotics and control	Antibiotics shortened duration of symptoms by about eight hours overall: trend for protection against rheumatic fever and glomerulo-nephritis. However, only six studies were conducted after 1980. Thirty children and 145 adults each must be treated with antibiotics to prevent one case of otitis media	Not reported owing to inconsistent recording in individual studies
Dagnelie <i>et al</i> <sup>2</sup>	Sore throat	RCT	239 patients clinically suspected of having streptococcal infection	Penicillin and placebo	Penicillin shortened symptoms by one to two days: no difference in daily activities between intervention groups. Benefit of penicillin confined to 46% of penicillin treated group who were found to have streptococcus on throat swab	About 5% had side effects, all in the penicillin group
Kaiser <i>et al</i> <sup>3</sup>	Common cold	RCT	314 patients with common cold	Co amoxiclav and placebo	Overall, the majority of people with colds do not benefit from antibiotics. A subgroup with nasal aspirates positive for certain bacteria benefited from co amoxiclav	23% for co amoxiclav, 5% for placebo
Little <i>et al</i> <sup>4</sup>	Sore throat	Open randomized trial	716 patients with sore throat and one physical sign	Ten days of penicillin, no prescription, or prescription after three days if symptoms not settling	No differences in recovery at three days, total duration of illness or time off work.	Not reported
Orr <i>et al</i> <sup>10</sup>	Bronchitis	Critical review of RCTs	Six trials involving 1279 patients with acute bronchitis	Tetracycline, trimethoprim-sulphamethoxazole, or erythromycin and placebo	No advantage to antibiotic treatment	Not reported
Verheij <i>et al</i> <sup>11</sup>	Bronchitis	RCT	140 patients with acute cough and purulent sputum	Doxycycline and placebo	Doxycycline shortens daytime cough by a mean of 1.5 days and by 4.1 days for people over 55	21% for doxycycline, 13% for placebo
King <i>et al</i> <sup>14</sup>	Bronchitis	RCT	140 patients with acute bronchitis, 91 randomized	Erythromycin and placebo	No significant differences in cough and other symptoms. However, erythromycin treated group missed less work (0.81 days versus 2.16 days)	36% for erythromycin, 15% for placebo
Becker <i>et al</i> <sup>12</sup>	Bronchitis	Systematic review	Eight trials involving 750 subjects aged over eight years old with a clinical diagnosis of acute bronchitis	Doxycycline, erythromycin, trimethoprim-sulfamethoxazole and placebo	Antibiotic treated subjects had slightly better outcomes	Antibiotic treated patients had significantly more adverse effects (odds ratio = 1.64)
Fahey <i>et al</i> <sup>13</sup>	Bronchitis	Systematic review	Nine trials of adults with acute cough	Antibiotic and placebo	No advantage to antibiotic treatment	Side effects more common with antibiotics (relative risk = 1.51)

**Table 1. (continued).** Summary of placebo-controlled trials and secondary studies from selected general medical and primary care journals and the Cochrane Data Base of Systematic Reviews published in the past five years of antibiotic treatment for sore throat, acute otitis media, maxillary sinusitis, and acute bronchitis.

Authors and publication year	Condition	Type of study	Subjects	Interventions	Outcome	Side effects
Del Mar <i>et al</i> <sup>6</sup>	Otitis media	Systematic review	Six studies of children with otitis media	Antibiotic and placebo	No difference at 24 hours; reduction of pain on second day in antibiotic treated group	Antibiotics double risk of vomiting, rash, and diarrhoea
Stalman <i>et al</i> <sup>7</sup>	Sinusitis	Evaluation of placebo-controlled, double-blind trials	Three studies	Antibiotic and placebo	One of three studies showed advantage for antibiotics: evidence supporting use of antibiotics in acute maxillary sinusitis in general practice is lacking	Not reported
Stalman <i>et al</i> <sup>8</sup>	Sinusitis	RCT	192 patients with symptoms and clinical signs of sinusitis	Doxycycline and placebo	No advantage for antibiotic treatment	17% for doxycycline
van Buchem <i>et al</i> <sup>9</sup>	Sinusitis	RCT	214 patients clinically suspected of having sinusitis by a GP and with radiographic abnormalities	Amoxycillin and placebo	No advantage for antibiotic treatment over one-year follow-up	28% for amoxycillin, 9% for placebo
Lindbaek <i>et al</i> <sup>7</sup>	Sinusitis	RCT	130 patients with clinical diagnosis of sinusitis confirmed on CT	Penicillin V, amoxycillin and placebo	86% receiving antibiotics reported cure on day 10, versus 57% receiving placebo. Median duration of symptoms was nine days for amoxycillin group, 11 days for penicillin group, and 17 days for placebo group. Over half placebo treated patients well or much better by day	More than half of patients in antibiotic treated groups reported some side effects, significantly more than the placebo group

associated with intention to reconsult<sup>4</sup> and with actual reconsulting with sore throat during the following year.<sup>34</sup>

### Microbial resistance

Perhaps the most urgent and serious consequence of the over-prescription of antibiotics is the development of bacterial resistance.<sup>35-37</sup> This has recently been recognized by the House of Lords Select Committee on Science and Technology.<sup>38</sup>

For patients themselves, recent use of antibiotics increases the likelihood of carriage of resistant pneumococci between two- and seven-fold.<sup>39</sup> Patients with acute otitis media or invasive disease caused by resistant pneumococci are significantly more likely to report the use of antibiotics within one week to three months before infection, compared with patients who have invasive disease caused by susceptible pneumococci. Recent use of antibiotics remains an independent predictor of invasive disease with resistant organisms, even after adjusting for risk factors such as younger age, being otitis prone, and underlying immunosuppressive disease.<sup>39</sup>

The use of antibiotics by one person also affects those in their immediate environment.<sup>40</sup> Housemates of patients treated with antibiotics for acne had large numbers of resistant organisms on their skin.<sup>41</sup> Over 50% of isolates of pneumococci from children attending day-care facilities were recently found to be resistant to penicillin,<sup>42</sup> and there are reports of invasive, resistant pneumococci being transferred between children in day-care settings.<sup>43</sup> Community-acquired methicillin resistant *Staphylococcus aureus* is appearing in children with no identified predisposing risk.<sup>44</sup>

The use of antibiotics in an individual has implications for larger populations, since resistance increases in proportion to the amount of antibiotics prescribed in the community.<sup>45,46</sup> *S. pneumoniae*, the leading cause of potentially life-threatening community-acquired disease, were universally sensitive to penicillin until 1967.<sup>47</sup> Resistance rates of over 20% are not unusual today, and multi-drug resistance is now common.<sup>39</sup> In Spain, where antibiotics are more freely available, the incidence of resistant pneumococci rose from 6% in 1979 to 44% in 1989.<sup>48</sup> Penicillin-resistant and multi-drug resistant strains of meningococcus are now emerging.<sup>49</sup>

There are no antibiotics to which resistance has not eventually emerged, and organisms resistant to one drug are likely to become resistant to others.<sup>40</sup>

### Solutions

Given this evidence, primary care physicians need to consider their levels of antibiotic prescribing. This may not be straightforward, since patients may have clear expectations of treatment based on how similar problems were dealt with in the past. A range of solutions may be available and there is a clear need for implementation and evaluation.

### Guidelines

The commonest response has been to promote guidelines and other education strategies.<sup>50,51</sup> This has yielded some positive results,<sup>52</sup> especially when clinicians were involved in the construction of guidelines locally.<sup>53</sup> The North of England Study of Standards and Performance in General Practice revealed that standards, set by doctors themselves, reduced the prescribing of antibiotics for children with acute cough by 11%, and by 10% for children with wheezy chests.<sup>54</sup> Evaluation of the implementation of guidelines developed by the Dutch College of General Practitioners shows that the percentage adherence to 10 different guidelines varied from 49% to 81%. Adherence to the standard

for otitis media was particularly good, with only 21% of patients receiving a prescription for an antibiotic.<sup>53</sup>

However, guidelines can never regulate for all the complexities of clinical practice,<sup>55</sup> and issuing a prescription can be a way for clinicians to cope in difficult situations.<sup>56</sup>

### *Enhanced consultation skills*

General practitioners report that prescribing antibiotics is the most common uncomfortable prescribing decision they make.<sup>57</sup> When patients expect antibiotics they are more likely to be prescribed,<sup>58</sup> and when physicians perceived that patients expect antibiotics, they are 10 times more likely to be prescribed.<sup>59</sup> There is still a widespread belief in Britain that a cough and discoloured sputum requires antibiotic treatment,<sup>22</sup> despite contrary evidence that has been in the literature for over 20 years.<sup>60</sup> Nearly 80% of adult Americans believe that antibiotics are indicated for a discoloured nasal discharge,<sup>33</sup> and physicians report that they are seven times more likely to prescribe antibiotics for a discoloured compared to a clear nasal discharge,<sup>61</sup> even though the appearance of nasal discharge does not predict the effectiveness of antimicrobial treatment.<sup>62</sup>

Clearly, biological factors alone do not explain current practice. Pressure of time, fear of damaging the doctor–patient relationship, avoiding home visits, and defensive medicine are some of the non-biomedical reasons for prescribing.<sup>30,50,57</sup> In-depth understanding of these non-biological pressures should inform interventions aimed at encouraging appropriate prescribing.

Perhaps both doctors and patients have a need to be doing ‘something active’ to treat infections, and antibiotics can be a way of helping some patients cope and are a symbol that their concerns have been taken seriously by the doctor.<sup>63</sup> Doctors need to go beyond explanations about the virus/bacteria distinction, and should leave patients feeling that their problems have been taken seriously and that they have been given ways of feeling more in control of the situation.<sup>63,64</sup>

Since physicians can assume that patients want antibiotics, when their main concern is for advice on symptomatic treatment and ruling out of more serious illness,<sup>65,66</sup> this research should aim to develop practical, brief ways for accurately assessing patient expectations, identifying their specific education needs, sharing information appropriately, and negotiating management that takes patient preferences seriously and are acceptable to both parties. The effect of exploring patients’ hypotheses about their illnesses (‘eliciting the patient’s differential diagnosis’) deserves further study,<sup>67</sup> being able to provide reassurance that an illness is not caused by a particular agent may sometimes be all that is required. Stewart *et al* has called this, ‘finding common ground’.<sup>68</sup>

### *Clinical diagnosis and identifying high-risk groups*

Clinical examination has a low predictive value in identifying those with a sore throat who are infected with bacteria,<sup>28</sup> and treatment based on throat swab results is often impractical,<sup>69</sup> expensive, and inaccurate.<sup>28</sup> There is also a low sensitivity and specificity for diagnosing sinusitis,<sup>70,71</sup> and factors other than infection can cause inflammation of the ear drum.<sup>31</sup> However, studies have shown that the absence of abnormalities on physical examination of the chest reduces the chances of pneumonia being present to a point where further diagnostic evaluation is unnecessary.<sup>72</sup> The search for robust and practical diagnostic criteria remains an important challenge, as does the identification of clinically useful predictors to identify groups at higher risk of more serious illness who will clearly benefit from antibiotics.<sup>73</sup> The summary of evidence suggests that some high-risk groups (older people with bronchitis, for example) do benefit from

antibiotics.<sup>11</sup> The Dutch NHG standard for treating otitis media in children recommends antibiotics in children over two years of age if symptoms persist beyond three days, and in children from six months to two years of age after 24 hours.<sup>74</sup> However, the problems of likely incidence of side-effects and impact on microbial ecology should be factored into cost–benefit analyses.

### *Patient information needs*

If patients engage in appropriate self care for these conditions, they will attend doctors’ surgeries less often, and thus reduce their chances of receiving unnecessary antibiotics. Work in the UK<sup>63</sup> and the US<sup>33,75,76</sup> shows that patients generally have little insight into the biomedical indications for antibiotics and the relationship between their personal use of antibiotics and the development of resistant organisms. More research into patients’ beliefs about antibiotics is needed to develop targeted self-care empowerment interventions that are appropriate to local beliefs.<sup>63</sup> Public health approaches that are not thoroughly developed can turn out to be expensive mistakes: the Ontario Ministry of Health spent \$500 000 on a patient education campaign about URTIs, which was sharply criticized for ignoring literature on compliance and for giving patients incorrect information.<sup>77</sup> Some information provision increases anxiety,<sup>78</sup> and the impact on parents’ knowledge of illness in children and their use of primary care services has proved disappointing in the UK.<sup>79–81</sup> Success in the US has also been mixed, with some interventions enhancing self care for URTIs,<sup>82</sup> some having no effect,<sup>83</sup> and some increasing physician visits.<sup>84</sup> Recently, patient leaflets were found to reduce re-attendance for lower respiratory tract illness.<sup>85</sup>

Opportunities for interventions with existing groups away from the stress of an acute illness (for example, parents bringing children for routine baby checks) could also be exploited.

### *Exploring non-antibiotic treatments for recurrent and chronic effects*

For a minority, these illnesses will not be self-limiting in the short-term, and some will experience frequent recurrences or chronic effects. Long-term antibiotics or repeated courses of short-term antibiotics are often used with marginal benefit in both chronic serous otitis media and recurrent acute otitis media.<sup>86–88</sup> Asthma management once focused almost exclusively on bronchospasm, but now the inflammatory component is emphasized, and other respiratory tract symptoms may be attributable more to inflammation than infection. Jones<sup>89</sup> screened 956 children and followed up cohorts with asthma and cohorts who tested positive for bronchial hyperreactivity. Both groups suffered more frequent upper respiratory tract infections and otitis media than controls. The pathophysiology of recurrent acute otitis media, recurrent sinusitis, and serous otitis media is similar and has an inflammatory basis,<sup>90</sup> since allergy or acute infections cause inflammation of the narrow passage to the sinus cavity or middle ear.<sup>91,92</sup> Intranasal steroids may improve Eustachian tube function, especially among atopic children: small, hospital-based studies have shown an advantage for intranasal steroids over placebo in chronic otitis media.<sup>93–96</sup> Intranasal use of sodium cromoglycate has recently been shown to rapidly improve congestive symptoms in URTIs.<sup>97</sup> To our knowledge, intranasal steroids and/or sodium cromoglycate (commenced as soon as URTI symptoms appear) has never been evaluated in preventing or treating acute otitis media. Again, anti-inflammatory drugs for serous otitis media have never been evaluated in a large primary care trial.

Certain patients with bronchitis benefit more from bronchodilators than antibiotics.<sup>98–100</sup> Anti-inflammatory drugs, com-



menced as soon as bronchitic symptoms appear, may provide additional advantage over bronchodilator or antibiotic treatment, but further trials are needed.

### Need for reappraisal

Future research in this field should therefore shift focus from why antibiotics should be used more selectively to effective strategies for changing physician and patient behaviour. There is evidence from Finland,<sup>46</sup> Iceland,<sup>101</sup> and Japan<sup>102</sup> that interventions can lead to changes in prescribing on a national level, and that this reduces levels of resistance to antibiotics. Some patient education strategies aimed at reducing consultations for URTIs have been effective.<sup>82,103</sup> Perhaps most encouragingly, evidence is accumulating that patient satisfaction does *not* fall among those who are not prescribed an antibiotic.<sup>4,67,104</sup> Not giving antibiotics to patients with a sore throat persuades one in four not to consult with the problem in the future, giving rise to the novel concept of 'numbers needed *not* to treat'.<sup>105</sup>

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